ATTACHMENT C

REMARKS

By this Amendment, Applicant amends the application to make some minor changes to the claims and specification in order to adopt the suggestions of the Examiner and overcome these minor objections. Applicants submit that the application in its present form overcomes all objections and rejections for the reasons as stated below.

In the Official Action, the Examiner made minor objections to the Specification and to the Claims on the basis of Section 112, second paragraph. Without addressing the merits of these objections, Applicant has overcome the rejections by the amendments herein.

In the Official Action, the Examiner rejected Claim 21 under 35 U.S.C. §102(b) as being anticipated by WO 89/06286 which is directed to dystrophin, described as the polypeptide product of the human MD locus, and is thus unrelated to the early developing liver proteins of the present invention. The Examiner argues that the two proteins have a short segment of 11 amino acids in common, and thus antibodies to the dystrophin would "meet the limitations of an antibody that binds to an amino acid sequence as set forth in SEQ ID NO:7" Such an assertion is incorrect, in particular in light of the fact that the dystrophin protein is roughly 4000 amino acids in length (see Fig. 8), and there is no indication whatsoever that the 11 amino acid region referred to by the Examiner is an antigenic site, much less one that would give rise to an antibody that recognizes a completely different protein. Accordingly, there is no teaching or suggestion that any antibody to dystrophin would be able to recognize and bind to the

protein of the present claims, and indeed the opposite is the case because of the vast differences between the proteins.

Even further, it has been determined that the antibodies recognizing the elf-3 protein recognize a unique region at the N-terminal end of the elf-3 protein. See the attached Abstract from Tang et al., *Oncogene* 21(34):5255-67 (August 2002). The epitope recognized by antibodies to elf-3 reveal that the binding site for the antibodies is at a unique region at the amino or N-terminal end, and thus shows that the unrelated 11 amino acid segment that the Examiner alleges is in common between dystrophin and elf-3 is not involved whatsoever in the antibody binding. Accordingly, the WO 89/06286 reference is unrelated to the present invention, and does not disclose or remotely suggest the present claims.

Applicants thus submit that the present application overcomes all prior rejections and has been placed in condition for immediate allowance. Such action is thus earnestly solicited.

END OF REMARKS

1: Oncogene. 2002 Aug 8;21(34):5255-67.

ELF a beta-spectrin is a neuronal precursor cell marker in developing mammalian brain; structure and organization of the elf/beta-G spectrin gene.

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Spectrins play a pivotal role in axonal transport, neurite extension, the organization of synaptic vesicles, as well as for protein sorting in the Golgi apparatus and cell membrane. Among spectrins there is great variability in sequence composition, tissue distribution, and function, with two known genes encoding the alpha-chain, and at least five encoding the beta-chain. It remains unclear as to whether novel beta-spectrins such as elf1-4 are distinct genes or beta-G-spectrin isoforms. The role for ELF in the developing nervous system has not been identified to date. In this study we demonstrate the genomic structure of elf-3, as well as the expression of ELF in the developing mouse brain using a peptide specific antibody against its distinctive amino-terminal end. Full genomic structural analyses reveal that elf-3 is composed of 31 exons spanning approximately 67 kb, and confirm that elf and mouse brain beta-G-spectrin share multiple exons, with a complex form of exon/intron usage. In embryonic stages, E9-12, anti-ELF localized to the primary brain vesicular cells that also labeled strongly with anti-nestin but not anti-vimentin. At E12-14, anti-ELF localized to axonal sprouts in the developing neuroblasts of cortex and purkinje cell layer of the cerebellum, as well as in cell bodies in the diencephalon and metencephalon. Double labeling identified significant co-localization of anti-ELF, nestin and dystrophin in sub ventricular zone cells and in stellate-like cells of the developing forebrain. These studies define clearly the expression of ELF, a new isoform of beta-G-spectrin in the developing brain. Based on its expression pattern, ELF may have a role in neural stem cell development and is a marker of axonal sprouting in mid stages of embryonic development.

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